DETAILED ACTION

The amendment filed Jan 5, 2009 has been entered. Claims 10 and 13 have been canceled. Claims 9, 11, 12 and 14 have been amended. After review and reconsideration, the finality if the Office action of July 24, 2008 has been withdrawn. Claims 1, 2, 4-9, 11, 12 and 14-16 are pending and under consideration.

As stated in the Office action of October 27, 2005, claims including p27 and p16 will not be afforded the earlier priority date of the provisional application 60/176,514 or 60/176,515 because neither of the '514 or '515 applications describe the instant method using the detection of p27 or p16. Thus, claims 12 and 14-16 have the effective priority date of January 12, 12, 2001.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 12 and 14 rejected under 35 U.S.C. 102(e) as being anticipated by Roninson et al (U.S. 2004/0058320).

Claim 12 is drawn to a method comprising the steps of (a) collecting a first tissue sample or cell sample from a breast cancer of an individual before exposing the individual to doxorubicin; (b) collecting a second tissue sample or cell sample from a breast cancer of an individual after exposing the individual to doxorubicin; (c) detecting in the first and second tissue sample or cell samples SA-Beta Gal activity, p21 expression, p27 expression, p16 expression of any combination thereof; and (d) determining whether SA-B-Gal activity, p21

expression, p27 expression, p16 expression or any combination thereof was increased following exposure to doxorubicin.

Roninson et al disclose a method comprising a method for monitoring the efficacy of treatment by detecting senescence associated markers in biopsy samples obtained after patient treatment (paragraph [0023] and paragraph [0048]). Roninson et al disclose (a)obtaining a biological sample comprising tumor cells from an animal before and after treatment; (b) comparing expression of at least one gene in Table I, 2A or 2B after treatment with expression of said gene or genes before treatment and(c) determining that said treatment has efficacy for treating the tumor if expression of at least one gene in 2A or 2B is higher after treatment, and expression of at least one gene in Table 1 is lower after treatment than before treatment (claims 86 and 87). Roninson et al disclose that p21 is up regulated (Table 2B). Roninson et al disclose that doxorubicin as a chemotherapeutic agent which can induce senescence in clinical samples (paragraphs [0004], [0007], [0042, second column, line 8] and [0059]. Roninson et al disclose a preferred embodiment wherein the gene in Table 2A is BTG1, BTG2, EPLIN, WIPI, Maspin, MIC-1, IGFBP-6 or amphiregulin (paragraph [0019]). Roninson et al disclose that induction of said genes is not limited to HCT116 cells treated cells because EPLIN which is down regulated in carcinoma cells is strongly up regulated in breast carcinoma cells after treatment with agents known to produce senescence-like growth arrest (paragraphs [0042] and [0089]). Roninson et al further disclose that Maspin is down regulated in advanced breast cancer (paragraph [0066]) consistent with the hypothesis that drug-induced growth arrest to tumor cells is maintained by a set of apparently redundant intracellular and paracrine factors (paragraph [0066]). Thus, it would be responsible to conclude that breast tumors were included in the "biological sample comprising tumor cells".

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roninson et al (U.S. 2004/0058320, priority to 60/257,907 filed December 21, 2000) in view of Bacus (U.S. 4,741,043, cited in a previous Office action).

Claim 14 embodies the method of claim 12 wherein SA-B-Gal, p21 or a combination thereof is detected. Claim 15 embodies the method of claim 12 wherein the detecting comprises staining the first and second tissue or cell sample for SA-Beta-Gal activity, p21, p27, p16, or any combination thereof, and measuring the optical density of one or more stained cells.

Roninson et al teach that expression of the corresponding genes in Table 2 can be measured at the protein level, using antibodies against the corresponding gene products for in situ immunostaining (paragraph [0048]), which meets the limitation of "stained cells" in claim 15. Roninson et al do not specifically teach determining the "optical density" or one or more stained cells. Claim 16 embodies the method of claim 15 wherein the optical density of the stained cells is measure by image analysis.

Bacus teaches the determination of optical density by image analysis (column 2, lines 28-29). Bacus teaches that image analysis overcomes staining differences due to ah to batch variations in stains (column 2, lines 16-42). Bacus teaches that image analysis is applicable to the analysis of cells as "objects" and in particular to the binding of a monoclonal antibody conjugated to a stain (column 3, lines 42-57).

It would have been prima facie obvious at the time that the claimed invention was made to analyze the optical density resulting from the in situ immunostaining of biopsy samples of Roninson et al by image analysis. One of skill in the art would have been motivated to do so by the teachings of Bacus on the advantages of image analysis for analyzing cells bound by a monoclonal antibody conjugated to a stain.

All other rejections and objections as set forth or maintained in the prior Office action are withdrawn in light of applicant's amendments.

Claims 1, 2, and 4-9 are free of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Karen A Canella/
Primary Examiner, Art Unit 1643